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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,874	11/14/2002	Jasmid Tanha	11054-1	8696

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NATIONAL RESEARCH COUNCIL OF CANADA
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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,874	TANHA ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-40* is/are pending in the application.

4a) Of the above claim(s) *10-24 and 31-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-9 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/15/2005 has been entered.

2. Claim 4 has been cancelled.

Claim 5 has been amended.

Claims 11-24 and 31-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

3. Claims 1-9 and 25-30 are under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections

Objections/Rejections Withdrawn

6. The objections to claims 5 and 6 as being dependent upon a cancelled claim are withdrawn in view of the amendments to the claims.

7. The rejections of claims 1-3, 5-9 and 25-30 (parts b-e) under 35 U.S.C. 112, second paragraph, as being indefinite are withdrawn in view of the amendments to the claims and applicant's arguments.

8. The rejection of claims 1-3 and 25-29 under 35 U.S.C. 102(b) as being anticipated by Casterman et al is withdrawn in view of the Declarations of Dr. Arumugam Murugahandam and Dr. Jamshid Tanha providing evidence that the use of phagemid vectors taught by Casterman would not result in a library of single domain antibodies from a naïve llama having the requisite affinity or useful affinity.

Response to Arguments

9. The rejection of claims 1-3, 5-9 and 25-30 (part a) under 35 U.S.C. 112, second paragraph, as being indefinite for reciting "said fragments comprising fragments" is maintained.

The response filed 1/14/2005 has been carefully considered, but is deemed not to be persuasive. The response states that claim 1 has been amended to clarify and remove the phrase "said fragments comprising fragments". In response to this argument claim 1 still recites the phrase "said fragments comprising fragments" and it remains unclear whether the phrase means that the library of antigen-binding fragments further comprises fragments of the antigen-binding fragments or if the phrase means that some of the antigen-binding fragments in the library of antigen-binding fragments have the recited affinity.

10. The rejection of claims 1-3 and 25-29 under 35 U.S.C. 102(e) as being anticipated by Frenken et al [a] (U.S. Patent 6,399,763 B1) is maintained.

The response filed 1/14/2005 has been carefully considered, but is deemed not to be persuasive. The response submits Declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha providing evidence that the preparation of a library of single domain antibodies from a non-immunized camelid (i.e., naïve antibodies) having useful affinity requires phage vectors as opposed to phagemid vectors. The response argues that Frenken et al [a] refer to the use of phagemid vectors, not phage vectors and this is a very important distinction in view of the Declaratory evidence and the use of phage vectors distinguishes the present invention over the cited art. In response to this argument, Frenken et al [a] teach phage vectors (e.g., lambda, T4 and pHEN.5) for the expression of the heavy chain variable domains obtained from a non-immunized llama and the antigen-binding affinities of some of the antibodies in the phage library have dissociation constants (K_D) less than 100nM, which is less than 5.7×10^{-5} M (see column 5, lines 27-29, column 7, lines 50-54, column 8, lines 50-57 and column 9, lines 1-29 and example 1). The declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha have been carefully considered, but are insufficient to overcome the instant rejection because Frenken et al [a] teach phage vectors as discussed above and thus, the instant claims are not distinguished over Frenken et al [a].

Therefore, the rejection of claims 1-3 and 25-29 as being anticipated by Frenken et al [a] is maintained.

11. The rejection of claims 1-3 and 25-29 under 35 U.S.C. 102(a) as being anticipated by Frenken et al [b] (WO 99/37681) is maintained.

The response filed 1/14/2005 has been carefully considered, but is deemed not to be persuasive. The response submits Declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha providing evidence that the preparation of a library of single domain antibodies from a non-immunized camelid (i.e., naïve antibodies) having useful affinity requires phage vectors as opposed to phagemid vectors. The response argues that Frenken et al [b] refer to the use of phagemid vectors, not phage vectors and this is a very important distinction in view of the Declaratory evidence and the use of phage vectors distinguishes the present invention over the cited art. In response to this argument, Frenken et al [b] teach phage vectors (e.g., lambda, T4 and pHEN.5) for the expression of the heavy chain variable domains obtained from a non-immunized llama. Therefore, it remains the examiner's position that Frenken et al [b] have taught a phage library of antigen-binding antibody fragments, obtained from a non-immunized llama and cloned into a phage vector that is identical to the claimed phage library antigen-binding antibody fragments also obtained from a non-immunized llama and also cloned into a phage vector and therefore, the phage library of Frenken et al [b] is identical to that claimed and would necessarily comprise some heavy chain antibodies (antigen-binding antibody fragments) having an antigen binding affinity with a dissociation constant of 5.7×10^{-5} M or lower. The declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha evince that the use of phage vectors for obtaining a library of single domain antibodies (heavy chain antibodies) from

a non-immunized camelid (i.e., llama) necessarily produces single domain antibodies having useful affinity and the library would necessarily comprise single domain antibodies having a dissociation constant of 5.7 X 10^{-5} M or lower.

Therefore, the rejection of claims 1-3 and 25-29 as being anticipated by Frenken et al [b] is maintained.

12. The rejection of claims 1-3, 5-9 and 25-30 under 35 U.S.C. 103(a) as being unpatentable over Casterman et al in view of McCafferty et al and Krebber et al is maintained.

The response filed 1/14/2005 has been carefully considered, but is deemed not to be persuasive. The response argues as above for Casterman et al and submits evidence in the Declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha, arguing that Casterman would not have lead one skilled in the art in the direction of the claimed invention (i.e., phage vectors). Applicant does not argue the teachings of McCafferty et al or Krebber et al or the combination of the cited references in the instant obviousness rejection. Although Casterman does not apparently teach phage vectors, applicant is reminded that the instant rejection is based on the combination of the cited references and what they would have suggested to one versed in the art. References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969). Further, one cannot show non-obviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The response also argues that one skilled in the art would have employed phagemid vectors based on the teachings of Casterman et al and therefore would have been expected to fail in producing a library of antigen-binding antibody fragments having useful affinity and the cited references are insufficient to direct one skilled in the art toward the use of phage vectors. Again, the instant rejection is based on the combined teachings of Casterman et al and McCafferty et al and Krebber et al and what the combined teachings taken as a whole would have suggested to one of ordinary skill in the art at the time the invention was made. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case the teachings of Krebber et al pertaining to the difficulties in obtaining high phage titers using the fd-tet phage vector carrying a tetracycline resistance gene and the teachings of Krebber also indicating success when inserting the ampicillin and chloamphenicol resistance genes individually in the fd-tet phage vector and selecting with the appropriate antibiotic to produce fd-tet phage having high phage titers (i.e., at least 10^9 and 10^8 pfu/ml) and the teachings of McCafferty indicating success in using the fd-tet phage vector for phage expression of antibodies obtained from a non-immunized animal

would have led one of ordinary skill in the art at the time the invention was made to combine the references with the teachings of Casterman et al to produce a phage display library of antibodies obtained from a non-immunized llama and use the fd-tet phage vector to obtain high phage titers. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144. Further, in view of the evidence submitted in the declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha, a phage library of antigen-binding antibody fragments, obtained from a non-immunized llama and cloned into a phage vector would necessarily comprise some heavy chain antibodies (antigen-binding antibody fragments) having an antigen binding affinity with a dissociation constant of 5.7×10^{-5} M or lower.

Therefore, the rejection of claims 1-3, 5-9 and 25-30 under 35 U.S.C. 103(a) as being anticipated by Casterman et al in view of McCafferty et al and Krebber et al is maintained.

13. The rejection of claims 1-3, 5-9 and 25-30 under 35 U.S.C. 103(a) as being unpatentable over Frenken et al [a] in view of McCafferty et al and Krebber et al is maintained.

The response filed 1/14/2005 has been carefully considered, but is deemed not to be persuasive. The response argues as above for Frenken et al [a], i.e., Frenken et al [a] teach phagemid vectors and not phage vectors and submits the Declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha establishing that the use of a phagemid vector would not produce the library of antigen-binding antibody fragments having useful binding affinity as claimed. In response to this argument and as argued above, Frenken et al [a] teach phage vectors (i.e., lambda, T4 and pHEN.5) for the expression of the heavy chain variable domains (antigen-binding antibody fragments) obtained from a non-immunized llama and the antigen-binding affinities of some of the antibodies in the phage library have dissociation constants (K_D) less than 100nM, which is less than 5.7×10^{-5} M (see column 5, lines 27-29, column 7, lines 50-54, column 8, lines 50-57 and column 9, lines 1-29 and example 1). Further, in response to applicant's arguments against Frenken et al [a] separately, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The response also argues that one skilled in the art would have employed phagemid vectors based on the teachings of Frenken et al [a] and therefore would have been expected to fail in producing a library having fragments with useful affinity and the recited references are insufficient to direct one skilled in the art toward the use of phage vectors. Although applicant did not argue the combination of the references cited in the instant obviousness rejection, the following is reiterated for applicant's convenience.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a phage library antigen-binding antibody fragments, obtained from a non-immunized llama and cloned the antigen-binding antibody fragments into the fd-tet phage vector in the absence of tetracycline because according to Krebber et al fd-tet phage carrying the tetracycline resistance gene yields low phage titers and higher phage titers (i.e., at least 10^9 and 10^8 pfu/ml) are obtained when using fd-tet in the absence of tetracycline (i.e., selection with ampicillin or chloamphenicol). Thus, there would be an advantage of using the fd-tet phage vector in the absence of tetracycline for producing a high titer phage library of antigen-binding antibody fragments obtained from a non-immunized llama and one of ordinary skill in the art would have had a reasonable expectation of success in doing so in view of the teachings of McCafferty et al indicating success in using the fd-tet vector for bacteriophage or phage expression of antibodies obtained from a non-immunized animal. Further, in view of the evidence submitted in the declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha, a phage library of antigen-binding antibody fragments, obtained from a non-immunized llama and cloned into a phage vector would necessarily comprise some heavy chain antibodies (antigen-binding antibody fragments) having an antigen binding affinity with a dissociation constant of 5.7×10^{-5} M or lower.

Therefore, the rejection of claims 1-3, 5-9 and 25-30 under 35 U.S.C. 103(a) as being anticipated by Frenken et al [a] in view of McCafferty et al and Krebber et al is maintained.

14. The rejection of claims 1-3, 5-9 and 25-30 under 35 U.S.C. 103(a) as being unpatentable over Frenken et al [b] in view of McCafferty et al and Krebber et al is maintained.

The response filed 1/14/2005 has been carefully considered, but is deemed not to be persuasive. The response argues as above for Frenken et al [b], i.e., Frenken et al [b] teach phagemid vectors and not phage vectors and submits the Declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha establishing that the use of a phagemid vector would not produce the library of antigen-binding antibody fragments having useful binding affinity as claimed. In response to this argument and as argued above, Frenken et al [b] teach phage vectors (e.g., lambda, T4 and pHEN.5) for the expression of antigen-binding antibody fragments (i.e., heavy chain variable domains) obtained from a non-immunized llama. Thus, it remains the examiner's position that Frenken et al [b] have taught a phage library of antigen-binding fragments, obtained from a non-immunized llama and cloned into a phage vector that is identical to the claimed phage library of antigen-binding antibody fragments also obtained from a non-immunized llama and also cloned into a phage vector and therefore, the phage library of Frenken et al [b] necessarily comprises some heavy chain antibodies (antigen-binding antibody fragments) having an antigen binding affinity with a dissociation constant of 5.7 X 10^{-5} M or lower. The declarations of Dr. Arumugam Muruganandam and Dr. Jamshid Tanha evince that the use of phage vectors for producing a phage library of antigen-binding antibody fragments obtained from a non-immunized camelid (i.e., llama) necessarily produces single domain antibodies (antigen-binding antibody fragments)

having useful affinity and the phage library would necessarily comprise single domain antibodies having a dissociation constant of 5.7 X 10^{-5} M or lower.

The response also argues that one skilled in the art would have employed phagemid vectors based on the teachings of Frenken et al [b] and therefore would have been expected to fail in producing a library having fragments with useful affinity and the recited references are insufficient to direct one skilled in the art toward the use of phage vectors. Although applicant did not argue the combination of the references cited in the instant obviousness rejection, the following is reiterated for applicant's convenience. One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a phage library antigen-binding antibody fragments, obtained from a non-immunized llama and cloned into the fd-tet phage vector in the absence of tetracycline because according to Krebber et al fd-tet phage carrying the tetracycline resistance gene yields low phage titers and higher phage titers (i.e., at least 10^9 and 10^8 pfu/ml) are obtained when using fd-tet in the absence of tetracycline. Thus, there would be an advantage of using the fd-tet phage vector in the absence of tetracycline for producing a high titer phage library of antigen-binding antibody fragments obtained from a non-immunized llama and one of ordinary skill in the art would have had a reasonable expectation of success in doing so in view of the teachings of McCafferty et al indicating success using the fd-tet vector for phage expression of antibodies obtained from a non-immunized animal.

In response to applicant's arguments against Frenken et al [b] separately, one cannot show non-obviousness by attacking references individually where the rejections

are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Therefore, the rejection of claims 1-3, 5-9 and 25-30 under 35 U.S.C. 103(a) as being anticipated by Frenken et al [b] in view of McCafferty et al and Krebber et al is maintained.

15. The rejection of claims 1-3, 5-9 and 25-30 under 35 U.S.C. 103(a) as being unpatentable over Hoogenboom in view of Lauwereys et al and Krebber et al is maintained.

The response filed 1/14/2005 has been carefully considered, but is deemed not to be persuasive. The response did not argue the instant obviousness rejection of Hoogenboom et al in view of Lauwereys et al and Krebber et al, however, the following is reiterated for applicant's convenience.

The teachings of Hoogenboom et al and Lauwereys et al and Krebber et al have been described in the previous Office Action (see item no. 23 beginning at page 21 and the top of page 15 of the Office Action mailed 11/15/2004).

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a phage display library of VHH antibodies as potent enzyme inhibitors as taught by Lauwereys et al and to have obtained the VHH antibodies from a non-immunized llama (i.e., naïve VHH) since immunization is not always ethically possible, nor always effective for non-immunogenic

and toxic antigens as taught by Hoogenboom et al and it would have been obvious to have used fd-tet phage in the absence of tetracycline for higher phage library titers (i.e., greater than 10^9 pfu/ml) as taught by Krebber et al because Hoogenboom et al teach al teach cDNA libraries and phage display libraries of antibodies from non-immunized animal sources and immunized sources are not always ethically possible, neither always effective due to tolerance mechanisms towards or toxicity of antigen and phage display libraries of naïve antibodies that are sufficiently large and diverse can be used to generate antibodies to a large panel of antigens, including self, non-immunogenic and toxic antigens and Lauwereys et al teach that VHH antibodies obtained from llamas are potent enzyme inhibitors and are better suited for intracellular immunization compared to conventional scFvs due to their superior enzyme-neutralizing capacity. Thus, there would be an advantage to using VHH antibodies obtained from llamas. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a phage display library of VHH antibodies as potent enzyme inhibitors as taught by Lauwereys et al and to have obtained the VHH antibodies from a non-immunized lama (i.e., naïve VHH) since immunization is not always ethically possible, nor always effective for non-immunogenic and toxic antigens as taught by Hoogenboom et al and it would have been obvious to have used the fd-tet phage vector in the absence of tetracycline for higher phage library titers (i.e., greater than 10^9 pfu/ml) as taught by Krebber et al because Hoogenboom et al and Krebber et al teach fd-tet phage and Krebber et al teach that fd-tet phage carrying a tetracycline resistance gene, yielded rather low phage titers, and higher phage titers (i.e., greater

than 10^9 and 10^{10} pfu/ml) can be obtained using fd-tet phage generated in the absence of tetracycline (see table 1). Thus, there would be an advantage to using the fd-tet phage vector in the absence of tetracycline and, it would have been obvious to the ordinary skilled artisan to generate a phage display library in the absence of tetracycline to obtain higher phage titers because phage display libraries of naïve antibodies that are sufficiently large and diverse can be used to generate antibodies to a large panel of antigens, including self, non-immunogenic and toxic antigens and immunized sources are not always ethically possible. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed phage library of antigen-binding antibody fragments obtained from a non-immunized llama and cloned into a phage vector with the phage library of antigen-binding antibody fragments also obtained from a non-immunized llama and also cloned into a phage vector (i.e., fd-tet phage vector) of the prior art, the burden of proof is upon the Applicant to show an unobvious distinction between the structural and functional characteristics of the claimed phage library of antigen-binding antibody fragments from a non-immunized llama cloned into a phage vector and the phage library of antigen-binding fragments from a non-immunized llama cloned into a phage vector of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a phage display library of VHH antibodies as potent enzyme inhibitors as taught by Lauwereys et al and to have obtained the VHH antibodies from a non-immunized llama (i.e., naïve VHH) since immunization is not

always ethically possible, nor always effective for non-immunogenic and toxic antigens as taught by Hoogenboom et al and it would have been obvious to have used fd-tet phage in the absence of tetracycline for higher phage library titers (i.e., greater than 10^9 pfu/ml) as taught by Krebber et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

New grounds of Rejections

16. Claims 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The response filed 1/14/2005 has introduced NEW MATTER into the claims. Newly amended claims 5 and 6 recite that the phage library includes at least 8.8 X 10^8 different antigen-binding fragments and at least 10^8 different antigen-binding fragments. The response did not point out where support for amended claims 5 and 6 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore

specifically point out the support for any amendments made to the disclosure."). Page 12 of the originally filed disclosure apparently provides adequate written support for a library of antigen-binding antibody fragments of the size of approximately 8.8×10^8, however, there is insufficient written support for a library of 8.8×10^8 and 10^8 different antigen-binding antibody fragments. There is no indication or disclosure that each of the antigen-binding antibody fragments in the library are different. Thus, as amended, claims 5 and 6 now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in presently amended claims 5 and 6, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claim 54 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at

(571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER